

CONSTRUCTIVE EPIDEMIOLOGY.

BY

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THE services of medical men, pathologists, and parasitologists are required for investigating the nature of any disease, whether it occurs in isolated cases or in epidemics; but mathematicians are needed to examine the cause and progress of the latter—just as any skilled observers may trace the path of a planet, but careful mathematical computations must be made into the forces concerned in its movement. Such computations may be either deductive (*a posteriori*), or constructive (*a priori*). By the former we seek to deduce the laws from the observed facts; in the latter we assume what we suppose are the laws, and then try to verify them by inquiring whether they explain all the facts.

Twelve years ago the Royal Society published a paper by me on the *a priori* analysis of “happenings” including epidemics,⁷ and gave me a grant to enable me to acquire the valuable help of Miss Hilda P. Hudson, with whom I continued the paper to a second and third part; but though the paper received the attention of such distinguished mathematical students as M. Greenwood⁸ and A. J. Lotka,^{6 11 14} few medical writers appear to have noticed it, and some recent books on epidemiology do not mention it. Yet Greenwood said of it when the first part was published:

“Modern researches fall into two classes. On the one hand those directly or indirectly inspired by the epoch-making discoveries of Professor Karl Pearson in the theory of mathematical statistics; on the other, the independent investigations of Sir Ronald Ross.”

I should therefore like an opportunity to recall the attention of the profession to a subject which I hope will ultimately be of considerable service to it.

First, I should say that in 1904 I read a paper at the St. Louis Congress in America on the cognate subject of the random-scatter of individuals, such as men or mosquitos or any other living creatures issuing from a centre outwards in all possible directions. Not being a mathematician I could not solve the problem accurately; but I ascertained that most of the individuals would



probably die fairly close to the point from which they started (*British Medical Journal*, May 13th, 1906). The problem was afterwards taken up and accurately solved by Pearson and Blakeman.²

A few years later, when writing a report on malaria in Mauritius for the Government of that colony,³ at a time when few people understood the mosquito theory regarding the carriage of that or of other diseases, I thought it advisable to indicate mathematically how such diseases might increase or diminish with changes in the local numbers of the insects, however caused. My demonstration was rhetorical rather than rigid (Sections 11, 12, and 13), and was made on the theoretical assumptions that those numbers remain constant for the period under survey, and that every person concerned receives about the same number of mosquito bites in a month. Then, if the number of bites is large enough, the proportion of infected persons in a locality will rise; if it is small enough, the number of infected persons will fall; but if it stands at a certain figure, the total number of infected persons should also remain fixed. I called this fixed condition "static malaria."

By assuming certain constants (which have never been properly investigated) I calculated that the proportion of infected persons to the whole population of a locality should remain fixed if the proportion of carrying *Anopheles* to each person is about $\frac{40}{1-m}$ during one month, where m is the proportion of infected persons to the whole population at the beginning of the inquiry. Thus if m is very small to begin with, the number of *Anopheles* may still be up to about 40 per head of the human population during one month without any change taking place. That is, a locality should probably remain almost free of malaria, although there are as many as 40 mosquitos of a suitable malaria-carrying kind during one month to each human individual in the locality. If the number of *Anopheles* rises over about 40 to each human being in the area under consideration, and if there are by chance any suitable cases of malaria at all in the area, introduced by immigration or in transit, then the number of local cases is likely to begin to increase until it reaches a fixed limit depending on the average number of mosquitos per human being. We can form a rough estimate of that fixed limit (if my assumed constants are nearly right) by obtaining the value of m from the equation above—namely,

$$a = \frac{40}{1-m},$$

that is, from

$$m = 1 - \frac{40}{a}$$

where a denotes the number of *Anopheles* to each person in the locality during one month. Thus if $a=40$, $m=0$,

as already stated; but if $a=60$, m will probably rise to a limit of $1/3$ —meaning that one-third of the whole population will ultimately become infected with malaria if the number of *Anopheles* keeps at that figure, other conditions remaining the same. If $a=80$, half the entire population will probably become infected in time; and if a becomes very large, m will nearly equal unity—that is, almost the entire population—as often happens. Of course, m is not supposed to be capable of having negative values, which would be meaningless.

The principal point indicated by this calculation is that a comparatively small rise in the number of *Anopheles* per man, as the rise from 40 to 60 during one whole month, might nevertheless suffice to send up the malaria rate in a locality from zero to about one-third of the whole human population; which would amount to a serious outbreak. A rise from 40 to 80 *Anopheles* per man per month should ultimately increase the malaria rate from zero to half the population—which would constitute a grave epidemic. Yet such variations in the numbers of one kind of mosquito (only) would probably pass quite unnoticed even by educated residents, and also might possibly be masked by an abundance of other kinds which have nothing to do with malaria. It would be difficult or impossible to establish or even to estimate by observation alone any such a law of correlation between the number of the cases and the number of the carriers concerned.

It may be asked how exactly I computed the number 40 mentioned in the equations given above. It is a convenient integer representing the decimal fraction 39.61, which equals $4 \times 4 \times 4 \times 3 \times 0.2063$. I conjectured that not more than a quarter of any mosquitos present succeed in biting human beings (about half the number of mosquitos are males, which do not bite at all). Only a quarter of these will succeed in biting a second time, as required by the law of mosquito transmission. Only about one-third will live long enough (about one week) to mature the malaria parasites within them; and only about a quarter of the human cases of malaria will contain the sexual forms of the parasites required for mosquito transmission, at any given moment when a mosquito happens to bite. The fraction 0.2063 was, I calculated, the proportion of human cases of malaria which remain infected for a month when half the cases recover every quarter.

These figures may be inaccurate, and probably are so; but the main object of the inquiry is, not to calculate the exact point at which static malaria commences, but to show that there must be some such point when the new cases exactly balance the recoveries.

Of course, in practice, the number of *Anopheles* and of the bites given by them are sure to vary with rainfall and temperature—that is, with season; but this must be understood to be the case; and the simple equations given do not pretend to contain any more than a first approxima-

tion towards the facts. The mathematical method possesses the advantage of showing, not only the elements which contribute to a result, but also how and how much each element does so—a thing which can seldom be expressed in words alone without much circumlocution.

This work, first given in my report on the prevention of malaria in Mauritius,³ was repeated and improved in Sections 26, 27, 28 (pp. 151–164) of my book^{4 5}. The former was examined mathematically by H. Waite (*Biometrika*, vol. vii, No. 4, October, 1910); but his argument contained a flaw which I pointed out to Professor Karl Pearson, though Waite endorsed my work. Section 28 of my book just mentioned leads to a problem of repeated operations (iteration), but I did not solve it until 1918 (see my paper¹⁰).

A second edition of my book was required early in 1911, and I determined to add a fuller treatment of this mathematical study in a final addendum to the work. This constituted Section 66 of the second edition.⁵ This section consists of thirty-five pages, which contain nineteen sub-headings and fourteen sub-subheadings. It continued the theme much more exactly, and referred not only to malaria but to similar happenings. The section was called “Theory of Happenings.” The problem before me was as follows: Suppose that some kind of event happens in every unit of time to a given proportion of a population, while at the same time the same population is undergoing constant changes due to births, deaths, immigration, and emigration, at one rate for the affected and at another rate for the unaffected, what will be the numbers of the affected and the unaffected portions of the population respectively at the end of the period considered? Also, suppose that some of the affected portion are constantly reverting in unit of time, then again what will be the numbers of the affected and the unaffected groups at the end of a given period covering t units of time?

These problems led to two simultaneous equations in the finite calculus. The equations were solved and integrated by that calculus, and the solutions were examined in detail. As well known, the finite calculus possesses the advantage that the unit of time taken may be large or small. When it is infinitesimal the finite calculus merges into the infinitesimal calculus, as shown in subsection (7, ii) and the following paragraphs. I also dealt with happenings that were repeated in the same individuals, and went on to examine metaxenous (or heteroxenous) diseases—that is, diseases which are common to two kinds of hosts. The rest of the paper deals with many details, and confirms my previous quantitative studies of malaria in the same book, and also gives some calculated constants; then it goes on to deal with the infinitesimal treatment of the subject. The integrations were obtained and are given; but of course I should like to have dealt with the theme even more

copiously than I have done. Unfortunately the paper contains many misprints and omissions, and the author himself finds considerable difficulty in understanding parts of it.*

Some years later I thought it advisable to submit the same investigation to the Royal Society in the form of the infinitesimal calculus only. Not being so hard pressed for time, I was able to develop the subject considerably, and to introduce a special section for the kind of happenings which are connected especially with infectious diseases—namely, happenings which do not fall at a constant rate on a population, but one in which every infected person tends to infect a given number of healthy persons in his turn. What would be the respective numbers of the affected and the unaffected groups of the population in this case? Here also I was able to solve and to integrate the differential equations in twenty-six pages containing seven subheadings and twenty-five sub-subheadings; but of course both papers require some mathematical knowledge. The Royal Society published the paper⁷ in full, and was also kind enough to suggest Dr. Hilda P. Hudson as an expert mathematician to help me. Next year we brought out two succeeding parts of the same paper⁹ containing twenty-eight pages, six subheadings, and twenty sub-subheadings. Errata for Part I are corrected at the beginning of Part II.

All the equations must of course be examined from many points of view, and, though we could not consider different diseases in detail, we hoped that our paper would enable more precise studies to be made in the future. Unfortunately Dr. Hudson was called away for war work, and we have not touched the subject again until quite recently. We are now beginning to consolidate and summarize our previous studies and to develop them by means of the finite calculus, the infinitesimal calculus, and by the use of integral equations.

I should add that my paper⁷ demonstrated that the sick-to-healthy communication of infectious diseases and the exhaustion of susceptible persons were enough to explain the rise and fall of the characteristic bell-shaped curves of most epidemics—a point on which some doubt was being thrown at that time.

My bibliography contains references to several works, some of which have been examined by Lotka, but all of which I have not read at present. They seem to reach their conclusions by dropping various constants, which, of course, always renders equations more simple but diminishes their general applicability, epidemics of many diseases being modified by small factors which are often overlooked.

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* We are preparing corrected "pulls" of Section 66, and will be glad to supply copies on application.

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